Targeting Transcriptional and Epigenetic Reprogramming in Stromal Cells in Fibrosis and Cancer.

Journal: Cold Spring Harb Symp Quant Biol

Publication Year: 2016

Authors: Nasun Hah, Mara H Sherman, Ruth T Yu, Michael Downes, Ronald M Evans

PubMed link: 26801159

Funding Grants: Metabolically-driven epigenetic changes in iPSC reprogramming

Public Summary:
The basis of many human diseases arises from both genetic and epigenetic regulation. Recent advances in the understanding of the mechanisms underlying transcriptional and epigenetic regulation and their prevalence as contributors to a diverse range of human diseases have led us to focus on transcription and epigenetic changes in a variety of human disease conditions. Specifically, our recent studies in liver fibrosis and pancreatic cancer have demonstrated that the epigenetic regulation in hepatic stellate cells (HSCs) and pancreatic stellate cells (PSCs) significantly contributes to the progress in such diseases and presents great therapeutic potential. We show that the vitamin D receptor (VDR) acts as a master genomic suppressor in both HSC and PSC activation. The studies also have demonstrated that the VDR ligand reduces fibrosis and inflammation in a murine liver fibrosis and pancreatitis model. Although our current studies focus on characterizing the roles of VDR and regulatory regions within gene promoters and regulatory enhancers, we have expanded our effort to epigenetic mechanisms as major determinants of gene activation and repression in order to develop potential therapeutics to modulate stroma-associated pathologies including inflammation, fibrosis, and cancer.

Scientific Abstract:
The basis of many human diseases arises from both genetic and epigenetic regulation. Recent advances in the understanding of the mechanisms underlying transcriptional and epigenetic regulation and their prevalence as contributors to a diverse range of human diseases have led us to focus on transcription and epigenetic changes in a variety of human disease conditions. Specifically, our recent studies in liver fibrosis and pancreatic cancer have demonstrated that the epigenetic regulation in hepatic stellate cells (HSCs) and pancreatic stellate cells (PSCs) significantly contributes to the progress in such diseases and presents great therapeutic potential. We show that the vitamin D receptor (VDR) acts as a master genomic suppressor in both HSC and PSC activation. The studies also have demonstrated that the VDR ligand reduces fibrosis and inflammation in a murine liver fibrosis and pancreatitis model. Although our current studies focus on characterizing the roles of VDR and regulatory regions within gene promoters and regulatory enhancers, we have expanded our effort to epigenetic mechanisms as major determinants of gene activation and repression in order to develop potential therapeutics to modulate stroma-associated pathologies including inflammation, fibrosis, and cancer.